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Review Article

Unmasking *Vibrio vulnificus*: Emerging "flesh-eating bacteria" and its health implications

Galo Guillermo Farfán-Cano[1]*

[1]Rey Juan Carlos University, Spain; [2]Society of Infectious Diseases of Guayas (SIG) and University of Guayaquil, Ecuador; [3]Northern Guayaquil General Hospital "Los Ceibos", Ecuador

*Correspondence:

Galo Guillermo Farfán-Cano
Rey Juan Carlos University, Spain

E-mail address:
dr.galo.farfan.cano@gmail.com

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Abstract

Recent media reports in the USA have raised concerns about dubbing *Vibrio vulnificus* as the "flesh-eating bacteria," which is traditionally associated with *Streptococcus pyogenes*. This review aimed to explore *V. vulnificus* as an emerging pathogen, its role in human infections, and its association with necrotizing fasciitis in wound infections. A systematic review was conducted of articles published between 2013 and 2023, focusing on *V. vulnificus* and its role in human infections. The inclusion and exclusion criteria were rigorously applied. The search identified 16 articles of which seven studies included in the review, with 77 *V. vulnificus*-induced necrotizing fasciitis cases reported over the past decade. Demographic and diagnostic data were analyzed, highlighting the need for further research due to regional variations. This comprehensive review highlights the emerging significance of *V.vulnificus* as a pathogen, particularly in the context of necrotizing fasciitis and emphasizes the need for region-specific research. Understanding *V. vulnificus* infection is crucial for timely intervention and improved public health outcomes.

Keywords: Flesh-eating bacteria, *Vibrio vulnificus*, review, necrotizing fasciitis, emerging infection

Introduction

In recent reports from the United States throughout the summer of 2023, numerous media outlets raised alarms within the general community by referring to *Vibrio vulnificus* as the "flesh-eating bacteria" (CDC, 2023a). This nomenclature is traditionally associated with *Streptococcus pyogenes*, a well-known pathogen responsible for severe skin and soft tissue infections, including necrotizing fasciitis (CDC, 2023b). While *S. pyogenes* has historically held the title of etiologic agent of "flesh-eating disease" due to its capacity to destroy tissue and induce necrosis in severe infections, *V. vulnificus* has emerged as a notable pathogen causing concern.

The surge in media reports labelling *V. vulnificus* as the "flesh-eating bacteria" warrants a comprehensive exploration of the scientific evidence surrounding this pathogen (CDC, 2023b). The aim of this review was to illuminate the evolving understanding of *V. vulnificus* as an emerging pathogen, its role in human infections, and its association with necrotizing fasciitis in wound infections. By synthesizing microbiological descriptions and analyses from scientific studies, we endeavored to provide a nuanced perspective on *V. vulnificus* and its potential significance in the context of necrotizing fasciitis. This scientific inquiry is driven by the urgent necessity to gain a better understanding of this emerging pathogen and its potential implications for public health.

Methods

The study design and criteria for inclusion and exclusion were implemented following a rigorous methodology to ensure the selection of pertinent articles and scientific novelty in the review of *V. vulnificus* in relation to necrotizing fasciitis, as well as its designation as the "flesh-eating bacteria" in response to media reports.



The inclusion criteria of the articles included were: (1) scientific articles and open-access reports published between 2013 and 2023; (2) research on *V. vulnificus* and its role as an infectious agent in humans; (3) studies addressing the characterization of *V. vulnificus* as the "flesh-eating bacteria" for necrotizing fasciitis; and (4) studies containing microbiological descriptions and analysis synthesis of *V. vulnificus*.

The exclusion criteria of the study were: (1) studies unrelated to *V. vulnificus* or its role in human infections; (2) studies not addressing the designation of *V. vulnificus* as the "flesh-eating bacteria" in the context of necrotizing fasciitis and (3) investigations lacking relevant microbiological descriptions or analysis synthesis.

Medical Subject Headings (MeSH) terms were meticulously selected to ensure the inclusion of articles related to *V. vulnificus* and its association with necrotizing fasciitis. The search was conducted between August 1 and September 1, and the results were collected on 21 September, 2023.

At initial stage, an extensive search was conducted in relevant databases and registers. The total number of records meeting the search criteria was identified, both in the databases and registers. Duplicate records were checked for and removed, resulting in a refined list of unique records. The unique records were selected based on predefined inclusion and exclusion criteria. Records that did not meet the criteria, such as those not exploring *V. vulnificus* in relation to human infections or those not available in open access, were excluded. After applying the inclusion and exclusion criteria, the number of records that met the requirements and were eligible for inclusion in the review was determined. Records that met all criteria and provided relevant information on the relationship between *V. vulnificus* and human infections were selected and included in the systematic review.

Results

The search yielded a total of four articles from PubMed and 12 articles from Scopus. One article was duplicated across both databases and was consequently excluded from the review. Furthermore, two additional articles were excluded owing to their unavailability in open access, and six articles were omitted because they did not address the microorganism *V. vulnificus* (Figure 1).

The compilation of the studies yielded a range of reported data on cases, published date sample types, and diagnostic methods (Table 1). Out of the total seven studies, there studies were original article, three studies were care report and one study review article consting the case.

Table 1. Characteristic of the article included in the systematic review

n	Author	Date	Type	Open access
1	Bhat et al.	2019	CR (Case report)	Yes
2	Cheng et al.	2023	OA (Original article)	Yes
3	D´Souza et al.	2018	CR (Case report)	Yes
4	Lee et al.	2019	OA (Original article)	Yes
5	Madiyal et al.	2016	CR (Case report)	Yes
6	Tomenchok et al.	2020	RA (Review article)	Yes
7	Tsai et al.	2019	OA (Original article)	Yes

In the last 10 years, three cases of necrotizing fasciitis caused by *V. vulnificus* have been reported in India, whereas 77 cases have been reported in Taiwan (Figure 2). There are no reported cases from other countries have been reported during 2013 and 2023.

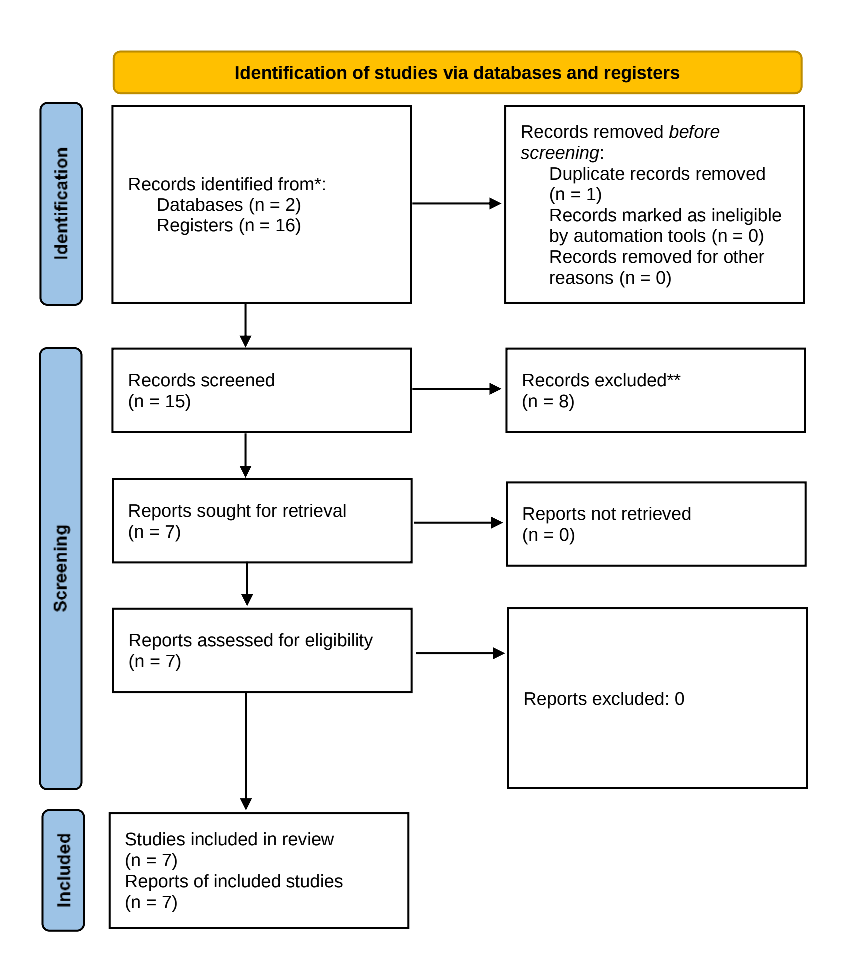


Figure 1. The process of record selection and filtering from the initial search stage to the inclusion of eligible records in the systematic review followed the PRISMA 2020 criteria.

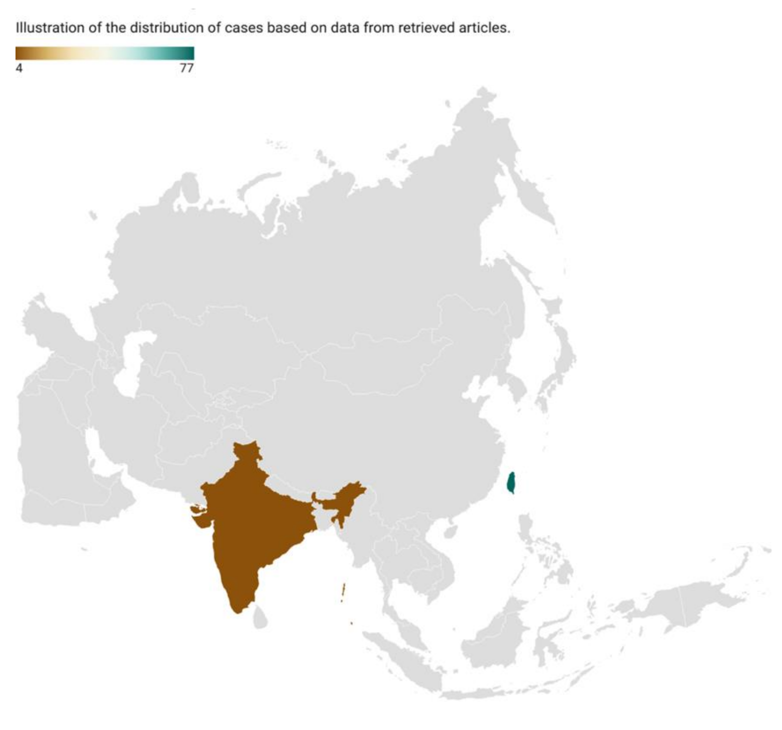


Figure 2. Illustration of the distribution of reported *Vibrio vulnificus* cases as etiological agents of necrotizing fasciitis based on data from various studies conducted over the last decade.

Table 2. Comprehensive profile of *Vibrio vulnificus* infection cases: Demographics, samples, diagnostics, and confirmatory methods

Author	Sample	Age	Sex	Comorbidities	Country	Diagnosis	Culture or Diagnostic Method	n	Resistant report	Treatment	Doses	Interval in hours	Mortality
Bath et al.	1	52	Male	Diabetes Liver disease Chronic alcoholism Smoker	India	NF	5% sheep blood agar & MacConkey agar	1	Ampicilin	Pip/Taz Amikacin Vancomicin	2,25 g 750 mg 1 g	6 36 12	1
Chen et al.	12	NS	NS	NS	Taiwan	NF	Multiplex polymerase chain reaction (PCR)	12	NS	NS	NS	NS	3
	1	67	Male	Diabetes	India	WI	Cellobiose polymyxin colistin (CPC) agar, PCR	2	NS	Pip/Taz	4,5	8	0
De Souza et al.	2	63	Male	Diabetes		WI	Cellobiose polymyxin colistin (CPC) agar, PCR		NS	Azithromicin	NS	NS	0
Lee et al.	49	NS	NS	NS	Taiwan	13 SMNF, 36 MONF	NS	49	NS	NS	NS	NS	NS
Madiyal et al.	1	52	Male	Alcoholic liver disease	India	Cellulitis	5% sheep blood agar, MacConkey agar; BacT/ALERT, Vitek 2 system	1	NS	Pip/Taz+Teicoplanin Doxycycline+Ceftazidime	4.5g 400mg 100mg+2g	12	0
Tsai et al.	99	NS	NS	NS	Taiwan	NF	Multiplex polymerase chain reaction (PCR)	BC CG 14, PCR BC 0 TS CG positive 16; PCR TS CG 14/16 positive TS NG positive 1/39, PCR BC 1	NS	NS	NS	NS	NS

NS: not specified (results of article analysis unpublished data or data not specific to *V. vulnificus*); NF: necrotizing fasciitis; WI: wound infection; SMNF: synchronous multifocal necrotizing fasciitis; MONF: monofocal necrotizing fasciitis; BC: blood culture; TS: tissue sample; CG: culture growth; NG: no growth. Tomenchok et al. we're not included in the present table, as the focus was on abrasions in children and not on microorganisms.

Table 2 presents a comprehensive profile of *V. vulnificus* infection cases from various studies, highlighting key demographic, diagnostic, and treatment-related aspects. The cases primarily involved male individuals aged 52–67 years. The presence of comorbidities such as diabetes, liver disease, chronic alcoholism, and smoking was notable in several cases (Table 2).

Based on the geographical distribution, the reported cases originated in India and Taiwan, suggesting regional variations in *V. vulnificus* infections. Most cases were diagnosed as necrotizing fasciitis (NF) or wound infection (WI), with the specific diagnostic method varying between studies. Multiplex polymerase chain reaction (PCR) and agar-based culture methods were used for the diagnosis. Based on the sample types, while cases specify the type of sample (blood culture or tissue samples), there is a lack of sample information (NS) in certain instances. Blood cultures and tissue samples are common diagnostic tools (Table 2).

In most of the cases antibiotics were administered in response to these infections. The antibiotics included ampicillin, piperacillin/tazobactam, amikacin, vancomycin, and azithromycin. The doses and dosing intervals varied among cases. From the cases the antibiotic susceptibility profiles are not consistently available across the cases (Table 2). It is important to note that the heterogeneous nature of these cases, including differences in diagnostic methods and antibiotic regimens, contributes to variations in the outcomes. Additionally, the emergence of *V. vulnificus* as a pathogen of concern in regions such as India and Taiwan underscore the need for further research and awareness regarding its clinical management and prevention. The data indicate a mortality rate of 4 out of 81 isolates over a ten-year period, accounting for 4.93% of the mortality among the cases (Table 2).

Discussion

Vibrios are a group of halophilic marine bacteria of various species found worldwide, primarily in warm coastal waters (CDC, 2023c; D'Souza et al., 2018). These bacteria are part of the normal bacterial flora in estuaries along the coast, and are commonly associated with seawater, seashells, and seafood (CDC, 2023c; D'Souza et al., 2018). *V. vulnificus*, a specific member of the *Vibrio* genus, has gained attention due to its implication in severe infections, particularly in high-risk individuals (CDC, 2023b, c; D'Souza et al., 2018; Tomenchok et al., 2020).

V. vulnificus causes life-threatening infections, particularly in individuals with underlying health conditions. *V. vulnificus* infections have been reported in various climate zones but are more prevalent in tropical and subtropical areas. This bacterium thrives in environments with temperatures above 20°C and salinities between 5 and 25 ppt. The primary modes of transmission for *V. vulnificus* are through the consumption of contaminated seafood, especially raw oysters, and the exposure of open wounds to seawater containing the bacterium.

Risk factors for infection

Several risk factors increase susceptibility to *V. vulnificus* infection. These include skin abrasions, chronic liver disease, immunodeficiency disorders, diabetes mellitus, cancer chemotherapy, and late-stage renal disease (Bhat et al., 2019; Madiyal et al., 2016; Tomenchok et al., 2020; Tsai et al., 2019). Additionally, occupational exposure, such as in the fishing industry, can increase risk (Bhat et al., 2019). Importantly, visible skin breaks or wounds are not always necessary for infection because minor abrasions may serve as entry points for the bacterium (D'Souza et al., 2018; Tomenchok et al., 2020).

Diagnostic methods

Prompt diagnosis is crucial in *V. vulnificus* infections because of their rapid progression and severity. Traditional culture-based methods require up to 48 hours to obtain definitive results, which can delay treatment initiation (Bhat et al., 2019; Cheng et al., 2023; Madiyal et al., 2016; Tsai et al., 2019). Molecular techniques, such

as PCR, have proven effective in detecting *V. vulnificus*, particularly when culture results are negative or rapid diagnosis is essential. DNA analysis of tissue samples has been shown to be more useful than that of blood samples for PCR analysis (D'Souza et al., 2018; Tsai et al., 2019).

Although culture-based methods are considered the gold standard for diagnosis, they are time-consuming and may miss cases with negative culture results (Bhat et al., 2019; Cheng et al., 2023; D'Souza et al., 2018; Lee et al., 2019; Madiyal et al., 2016; Tsai et al., 2019). Molecular methods, such as PCR, offer rapid detection, especially in culture-negative cases, but they require specialized equipment and training. Therefore, a combination of these approaches may provide the best diagnostic accuracy (D'Souza et al., 2018; Tsai et al., 2019).

Antimicrobial resistance and treatment

V. vulnificus infection is associated with high morbidity and mortality rates. Effective treatment involves the prompt initiation of appropriate antibiotics. *V. vulnificus* is susceptible to certain antibiotics such as doxycycline, minocycline, and third-generation cephalosporins such as ceftazidime. Combination therapies have been shown to be more effective than monotherapies in some cases (Bhat et al., 2019; Cheng et al., 2023; Madiyal et al., 2016).

Conclusion

V vulnificus is an emerging pathogen with the potential to cause severe infections, particularly in individuals with underlying health conditions. Early and accurate diagnosis, along with appropriate antimicrobial treatment, is essential for improving the outcomes of *V. vulnificus* infections. Molecular diagnostic methods such as PCR offer advantages in rapid detection; however, the awareness of healthcare providers and laboratory personnel is critical for timely intervention, especially in regions where these infections are less common.

Author contributions

Conceptualization: GGFC; Data Curation: GGFC; Formal Analysis: GGFC; Investigation: GGFC; Validation: GGFC; Writing – Original Draft Preparation: GGFC; Writing – Review & Editing: GGFC.

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Conflict of interest

There are no competing interests that exist.

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